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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,327	09/03/1999	SARAH ANNE ROBERTSON	A20-005	2475

26633 7590 06/20/2005

HELLER EHRMAN WHITE & MCAULIFFE LLP
1717 RHODE ISLAND AVE, NW
WASHINGTON, DC 20036-3001

EXAMINER

BELYAVSKYI, MICHAEL A

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/380,327

Applicant(s)

ROBERTSON ET AL.

Examiner

Michail A. Belyavskiy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 105-112, 115-125, 127- 132 and 134 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 105-112, 115-125, 127- 132 and 134 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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SUPPLEMENTARY OFFICE ACTION

This is a supplemental Office Action, in response to the amendment filed on 01/05/05 to address the issue raised in Applicant's arguments, filed on 01/05/05 with regards to the teaching of the references by Michel et al., and by Graham et al. Said references have not been considered in the previous Office Action, mailed on 03/24/05.

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (9 or (g) prior art under 35 U.S.C. 103(a).

2. Claims 105-112, 115-125, 127- 132 and 134 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,395,825 in view of Lea et al (Am J Reprod Immunol 34(1)), Nocera et al (Am J. Reprod. Immunology 33: 282-291, 1995); Clark et al (Hum Reprod 9(12): 2270-7, Dec 1994,), Thomas et al., (Am J Reprod. Immunol 644): 185-9, Dec 1984;), Thaler et al (Am J Reprod Immunol 21(3-4): 147-50, Nov-Dec 1989;) and Prakash et al., (Reproductive Immunology 70: 403-412, 1981) in view of the known fact disclosed in the Specification on overlapping pages 10-11 for the same reasons set forth in the previous Office Action, mailed on 03/24/05.

Applicant's arguments, filed 01/05/05 have been fully considered, but have not been found convincing.

Applicant asserts that one of ordinary skill in the art would have been expected that administering TGF- β to a prospective mother, either before or after attempted conception, would cause miscarriage. Applicant cited 3 references by Michel et al., and by Graham et al., (1992) and Graham et al., (1994) and Declaration under U.S.C. Rule 132 by Dr. Clark, filed on 07/15/04 to support this concept.

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Contrary to Applicant's assertion, the Examiner disagrees that "one of ordinary skill in the art would have been expected that administering TGF- β to a prospective mother, either before or after attempted conception, would **cause miscarriage**". It is noted that none of the cited references teaches or suggests that "administering TGF- β to a prospective mother, either before or after attempted conception, would **cause miscarriage**". Michel et al., only teach that the mechanism that prevent miscarriage are incompletely understood. Factors other than defective placental vasculature appear to associated with miscarriage in some women. How the miscarriage can be attributed to the hormonal disturbance of the underlying ovulatory disorder is not clear (see entire document, pages 984, 986 and 987 in particular). Graham et al., (1992) and Graham et al., (1994) teach that the purpose of the study was to determine whether TGF- β , normally found in the pregnant uterus has differential effects on *in vitro* proliferation and or invasiveness of human chorionic carcinoma cells compared to normal human first trimester trophoblast cells. The references teach that in contrast to normal trophoblast cells, TGF- β does not inhibit *in vitro* proliferation and invasiveness of two chorionic carcinoma cell lines (see entire documents , page 94 of Graham et al., 1994 in particular). Similarly, Declaration under U.S.C. Rule 132 by Dr. Clark filed on 07/15/04 only by analyzing the selected prior art references suggests that in his opinion at the time the invention was made it would have been thought that administration of TGF- β to a prospective mother, either before or after attempted conception, would cause miscarriage.

It is the Examiner's position, that none of the three references cited by Applicant teaches or suggests to one of ordinary skill in the art that administering TGF- β to a prospective mother, either before or after attempted conception, would cause miscarriage. Moreover, it appears that the Examiner and Dr. Clark differ on interpretation of both the claimed methods and the prior art teaching. As is evidenced by Tremellen and by Robertson references there is a different opinion for the role of TGF- β in miscarriage . In the article by Tremellen, it is clearly stated that " semen contains a powerful chemical called TGF- β , which signal the woman's immune system to greet those genetically foreign sperm with open arms rather than xenophobically bared teeth". A team of researchers begin studying **whether TGF- β can prevent recurrent miscarriage**. Similarly, Robertson teaches the **therapeutic potential of TGF- β** in human miscarriage. Clearly said references indicate that one of ordinary skill in the art **would not** expect that administering of TGF- β would cause miscarriage.

3. Claims 113 and 114 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,395,825 in view of Lea et al (Am J Reprod Immunol (34(1)), Nocera et al (Am J. Reprod. Immunology 33: 282-291, 1995) ; Clark et al (Hum Reprod 9(12): 2270-7, Dec 1994,), Thomas et al., (Am J Reprod. Immunol 644): 185-9, Dec 1984;), Thaler et al (Am J Reprod Immunol 21(3-4): 147-50, Nov-Dec 1989;) and Prakash et al., (Reproductive Immunology 70: 403-412, 1981;) in view of the known fact disclosed in the Specification on overlapping pages 10-11 as applied to claims 105-112, 115-125, 127- 132 and 134 above and further in view of Harlow et al., (of record, in A Laboratory Manual, Cold Spring Harbor Laboratory, page 61, 1988'), World Health Organization (of record, in World Health Organization Laboratory Manual for the

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Examination of Human Semen and Semen Cervical Mucus Interaction, Cambridge University Press, (NY 1987) and Martin-Villa et al (,Biol Reprod 5543): 620-9, Sept 1996,) for the same reasons set forth in the previous Office Action, mailed on 03/24/05.

4. Claim 126 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,395,825 (of record, May 1995; IDS in view of Lea et al (Am J Reprod Immunol 3441): 52-64, July 1995; PTO 892), Nocera et al (Am J. Reprod. Immunology 33: 282-291, 1995; PTO 892), Clark et al (of record, Hum Reprod 9412): 2270-7, Dec 1994, PTO 892), Thomas et al (Am J Reprod. Immunol 6(4): 185-9, Dec 1984; PTO 892), Thaler et al., (Am J Reprod Immunol 2143-4): 147-50, Nov-Dec 1989; PTO 892) and Prakash et al., (Reproductive Immunology 70: 403-412, 1981; PTO 892) in view of the known fact disclosed in the Specification on overlapping pages 10-11 as applied to claims 105-112, 115-125, 127- 132 and 134 above and further in view of Grainger et al (Nat Med 149): 932-7, Sep 1995; PTO 892) for the same reasons set forth in the previous Office Action, mailed on 03/24/05.

5. Claim 133 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,395,825 (of record, May 1995; IDS in view of Lea et al (Am J Reprod Immunol 3441): 52-64, July 1995; PTO 892), Nocera et al (Am J. Reprod. Immunology 33: 282-291, 1995; PTO 892), Clark et al (of record, Hum Reprod 9412): 2270-7, Dec 1994, PTO 892), Thomas et al (Am J Reprod. Immunol 6(4): 185-9, Dec 1984; PTO 892), Thaler et al., (Am J Reprod Immunol 2143-4): 147-50, Nov-Dec 1989; PTO 892) and Prakash et al., (Reproductive Immunology 70: 403-412, 1981; PTO 892) in view of the known fact disclosed in the Specification on overlapping pages 10-11 as applied to claims 105-112, 115-125, 127- 132 and 134 above and further in view of Heidenreich et al., (Am J Reprod Immunol 1994, 3142-3: 69-76,) for the same reasons set forth in the previous Office Action, mailed on 03/24/05.

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

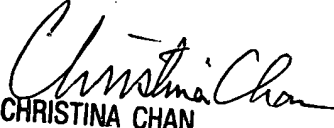
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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
June 13, 2005


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600